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ON NEPHRITIS OF MALARIAL ORIGIN.

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THE fact that albuminuria may occur in the course of malarial fever as well as during other acute infections is well known. Martin-Solon¹ estimated that it was to be found in a quarter of all cases. Laveran,² however, believes that this is a high percentage for the simple non-pernicious fevers. Joseph Jones³ refers to its occasional occurrence, but says: "In several hundred examinations of the urine of the different forms of malarial fever in the Marine Hospital at Savannah, Georgia, albumin was found in only one case, which was complicated with typhoid fever. This fact is important in its bearing upon typhoid and yellow fever." Anders,⁴ in 1780 cases collected from the records of various hospitals in Philadelphia, noted only eighteen instances in which albuminuria ("marked") was found. Hertz⁵ asserts that "it is no very uncommon thing to find albumin present in considerable quantities." . . . "Albumin is to be found in the urine either only on the fever days or during the intermission as well (fibrinous tube-casts have also been observed), and disappears on recovery." Atkinson⁶ studied the urine in seventy-six cases of intermittent and remittent fever, in which albuminuria occurred five times; in a second series, however, occurring during the late summer and fall of 1883, forty-five in number, albuminuria was noted in six instances. Kelsch and Kiéner⁷ assert that in ordinary malarial fevers "the presence of albumin is not rare in paroxysms of a certain intensity, but it is particularly common in relapses in old sufferers, where the kidney is

¹ *Gaz. Méd. de Paris*, 1848, iii. s., t. iii. Année, xix. 618.

² *Traité du Paludisme*, 1898, 8^o, Paris.

³ *Medical and Surgical Memoirs*, vol. ii. p. 772.

⁴ *Journal of the Amer. Med. Asso.*, 1895, vol. xxiv. p. 916.

⁵ *Ziemssen's Cyclopædia*, American edition, vol. ii. p. 641.

⁶ *Amer. Journ. Med. Sciences*, 1884, vol. lxxxviii. p. 149.

⁷ *Maladies des pays chauds*, p. 144.

already altered." They say that in the more severe bilious and gastric fevers (page 453) "albumin is frequent enough but inconsiderable and transient; it may be intermittent and disappear with the paroxysm, or it may continue during the intermission."

Despite the relative frequency with which some observers have noted albumin in the urine of malarial patients, its presence or absence has been used as a point in the differential diagnosis between certain forms of severe malaria and yellow fever, in which latter affection the early appearance of albumin is the rule. McLean, in *Reynolds' System of Medicine*, says: "Albuminous urine is almost invariable in yellow fever—only occasional in remittent." Again, of the urine in remittent fever, he says: "It seldom contains albumin . . . albuminous urine is the rule in yellow fever, a rare exception in remittent."

Ascoli,¹ Dubujadoux,² and others have noted the existence of pepturia in association with the malarial paroxysm.

The occurrence of acute nephritis in connection with malaria has also been recognized for many years: Chénouard,³ Hertz,⁴ Soldatov,⁵ Dewalsche,⁶ Verhaeghe,⁷ Schmid,⁸ Pepper,⁹ Busey,¹⁰ McLean,¹¹ Da Costa,¹² Wood,¹³ Rosenheim,¹⁴ Atkinson,¹⁵ Bermann,¹⁶ Stefaniowicz,¹⁷ Dods,¹⁸ and many others noting this condition.

Throughout the Southern States, as testified to particularly by the admirable records of Joseph Jones,¹⁹ the condition is not very infrequent. The grave and often fatal acute nephritis following haemoglobinuric attacks is well known. These cases have been well studied by Bastinelli²⁰ and Kelsch and Kiéner,²¹ who have described at length the changes in the kidneys following acute malaria. They believe that severe acute, diffuse, or glomerulo-nephritides may directly

¹ *Lav. d. Cong. d. Med. Int.*, 1892, Milano, 1893, vol. v. p. 350.

² *Arch. de Méd. et Pharm.*, Paris, 1892, p. 437.

³ *Rec. des travaux de la Soc. Méd. du Depart. d'Indre-et-Loire*, 2s, 1845, p. 101.

⁴ *Op. cit.*

⁵ *St. Pet. Med. Woch.*, 1878, iii. 345.

⁶ *Arch. Belges de Méd. Mil.*, 1859, xxiii. 20.

⁷ *Ibid.*, 1860, xxvi. 31.

⁸ *Deutsche Klinik*, 1852, 442.

⁹ *Amer. Journ. Med. Sci.*, 1866, li. 405, 408.

¹⁰ *Ibid.*, 1873, lxv. 123.

¹¹ *Op. cit.*

¹² *Med. Record*, N. Y., 1880, xvii. 54.

¹³ *Ibid.*, 1888, xxxiii. 820.

¹⁴ *Deutsch. med. Woch.*, 1886, xii. 752.

¹⁵ *Op. cit.*

¹⁶ *Internat. klin. Rundschau*, Wien, 1894, viii. 1844.

¹⁷ *Wien klin. Woch.*, 1893, vi. 365.

¹⁸ *Edinb. Med. Journ.*, 1888, xxxiii. ii. 1890.

¹⁹ *Op. cit.*

²⁰ *Ann. di Med. Navale*, Anno ii. 1896.

²¹ "Maladies des pays chauds," 8vo, Paris, 1889, and *Arch. de Phys. norm. et path.*, Paris, 1882, 2 s., ix. 278, 458.

depend upon the malarial infection. They assert that nephritis occurs in more than half the fatal cases. "It develops in cases where the disease has a relatively long duration and has been marked by symptoms of corpuscular dissolution, especially by haemoglobinuria, from which we may conclude that it depends less upon the direct action of the malarial poison on the kidney than upon the irritation produced in the gland by the passage of the haemoglobin and its derivatives."

Bignami,¹ in his valuable studies upon the anatomical alterations in acute malarial infections, noted the fact that the kidneys were, as a rule, but little affected. The glomeruli were markedly pigmented, the pigment granules sometimes being within large colorless cells, sometimes apparently within the endothelium of the glomerulus; at times, the most important lesions consisted of an exfoliation and degeneration of the epithelium lining the capsule; only in algid pernicious fever did he find glomeruli with very slight albuminous exudates. Sometimes, however, marked and extensive alterations of the parenchyma were found, consisting of focal necrosis of the epithelium, especially those of the tubuli contorti.

Barker,² in four fatal cases of malaria, found in three instances that the kidneys showed but few changes, consisting of a slight pigmentation of the glomeruli with albuminous exudates and casts, and a more or less swollen and degenerated condition of the epithelium of the convoluted tubules. A fourth instance was one of marked acute nephritis which was probably of malarial origin, although complicated later in its course by a streptococcus infection—Case II. of our series. In Anders'³ 1780 cases there were but four instances of acute nephritis.

The frequency of the occurrence of *chronic nephritis* as a result of malarial fever is a point about which different opinions have been held. Lenz⁴ and Rosenstein⁵ both believed malaria to be a frequent cause of chronic nephritis. Bartels⁶ was also a strong upholder of this idea. Herz⁷ likewise asserts that cases of acute nephritis in malaria may pass into a chronic diffuse process, a sequence which is recognized by many

¹ Atti della R. acc. med. di Roma, 1890, Anno xvi., s. ii., v. 317.

² Johns Hopkins Hospital Reports, 1895, v. 230.

³ Op. cit.

⁴ De diffusa nephritide chronica, præcipue respecto decursu morbi post intermittentem febrim, 80, Gryphiæ, 1865.

⁵ Path. u. Therap. der Nierenkrankheiten, Berlin, 1870, 215.

⁶ Ziemssen's Cyclopædia, Amer. edition, vol. xiv. p. 328.

⁷ Op. cit., p. 649.

observers. McLean¹ says: "I can confirm from personal observations Dr. Parke's remark that chronic Bright's disease is a consequence of ague. Many 'old Indians' who have suffered from malarial fevers die of this disease."

Kelsch and Kiéner² have described in detail the changes in chronic as well as in acute nephritis occurring in cases of old "fébricitants." They describe two main varieties of kidney as met with in chronic paludism: (1) the congested kidney; (2) the atrophic kidney.

1. The engorged kidneys are increased in size and weight and of firm consistency. The surface is smooth, the color deep red, the congestion being particularly marked in the pyramids. Owing to the extensive congestion of the vessels, interstitial hemorrhages or the escape of blood into the tubules may occur. There is a marked granular degeneration of the tubular epithelium, while desquamation is common. Hyaline casts may be found.

2. The atrophic kidneys are small, the surface is irregular, the capsule adherent, the consistency increased. The color is usually of a maroon or mahogany tinge, and often there is a blotchy appearance. Small cysts are common. Microscopically, alterations are to be found in the interstitial tissue as well as in the tubular epithelium. They note in conclusion³ that "malarial nephritides have but little that is characteristic about them. We may again, however, note: (1) The tendency toward hemorrhages in all forms and at all periods of the nephritis. (2) The frank character of the inflammation in contradistinction to the partly steatotic, partly sclerotic forms which gout and alcoholism give rise to so frequently with us. (3) The rarity, perhaps the absence of amyloid degeneration, the ordinary expression of septicæmia of all sorts. Even in the cachexias the fatty and colloid degenerations of the kidneys are of a subinflammatory character and give rise to hemorrhages. They are sharply distinguishable from the lesions of the senile kidney by the wholly secondary importance of the vascular changes, and notably by the absence of arterial atheroma."

Rowland⁴ noted the frequency of chronic nephritis in the malarial

¹ Reynolds' System of Medicine, vol. i.

² Maladies des pays chauds, 8vo, Paris, 1889, 744; Arch. de Phys. norm. et path., 1882, s. 2, t. ix. p. 278.

³ Arch. de Phys. norm. et path., 1882, s. 2, t. ix. 494.

⁴ The British Guiana Medical Annual and Hospital Reports, Demerara, 1892, 41.

regions of British Guiana. Laveran,¹ in his treatise, states that "acute or chronic nephritis is a fairly common complication of paludism. The nephritis has sometimes the characters of an epithelial nephritis (the urine contains albumin in great quantity, anasarca occurs and becomes rapidly generalized), sometimes those of interstitial nephritis or of mixed nephritis; this last form is, I believe, the commonest."

Other observers have paid very little attention to malaria as a cause of chronic renal changes. Thus, it is not mentioned in Senator's² work as an etiological factor in chronic nephritis. Anders,³ in 1780 cases of malaria, met with chronic nephritis in but one instance. Bignami,⁴ in his admirable studies on the pathological anatomy of chronic malarial infections, lays but little stress on the changes in the kidneys.

Marchiafava and Bignami⁵ have described amyloid degeneration of the kidneys following long and repeated febrile attacks. These cases had been associated with clinical and anatomical manifestations of a severe chronic nephritis. Beside the affection of the vessels of small and medium size and of the glomeruli, the authors found a considerable involvement of the walls of the renal tubules themselves.

Rem Picci,⁶ of Rome, has recently published an interesting communication upon the renal lesions in malarial fever, which has come to the author's observation since the writing of this paper. He recognizes the fact that a malarial infection may be the cause not only of simple albuminuria, but of extensive renal changes, although such cases are rare. Malarial nephritis occurs more commonly in the fall than in the spring, and is particularly common in young individuals. It occurs in both the severe and the mild forms of the disease, and is no more frequent, apparently, in the former than in the latter.

The attack is usually mild and of favorable outcome, but it may be severe, and in some instances passes into a chronic form. The symptoms of nephritis appear not only during the malarial attack, but sometimes develop after the disappearance of the symptoms of the

¹ Op. cit., p. 213.

² Die Erkrankungen der Nieren, Wien, 8vo, 1896. (Excerpt from Spec. Path. u. Therap., herausgegeben v. Nothnagel.)

³ Op. cit.

⁴ Boll. d. R. acc. Med. d. Roma, 1893, xix. 186.

⁵ Riforma Medica, 1891, Anno vii., vol. i. 571.

⁶ Il Policlinico, vol. v-M., 1898, 197.

infection. These cases Rem Picci has termed "post-malarial." Amyloid degeneration is occasionally met with. The exciting cause of malarial nephritis is believed by the author to be the irritation of the kidney due to the elimination of the toxic products of the infection.

Thus, in summary, it may be seen that the association of albuminuria with malarial fever has been generally recognized, but its frequency variously estimated, the general tendency being toward the idea that, even in severe forms, it is not so common but that the early appearance of albuminuria may be regarded as a valuable point in the differential diagnosis between this disease and yellow fever. And while acute nephritis dependent upon malarial infection is well understood to occur, there are no existing statistics tending to show its relative frequency as compared with nephritis in other acute infections. The same may be said with regard to the more chronic renal changes. It has therefore seemed advisable to us to analyze our cases of malarial fever occurring during the last eight years, with a view to determining the following points :

1. The frequency of albuminuria in malarial fever as compared with other acute infections.
2. The frequency of acute nephritis in malarial fever.
3. The possible influence of malarial fever in the production of chronic renal changes.

ALBUMINURIA.

During the past eight years 758 cases of malarial fever have been treated in the wards of the Johns Hopkins Hospital. In 691 of these cases there are records of examination of the urine.

Albumin was present in 321 instances—46.4 per cent.

There was no albumin in 370 instances—53.5 per cent.

In the great majority of cases the albumin was present as a small trace.

Casts of the urinary tubules were found in 121 cases—17.5 per cent.

The proportion of cases in which albuminuria was present varied materially, as might have been expected, according to the type of fever.

TABLE OF 691 CASES IN WHICH AN EXAMINATION OF THE URINE
WAS RECORDED.

Tertian fever—344 cases:

Albumin present in	.	.	.	132 cases.—38.3 per cent.
No albumin	"	.	.	212 " 61.6 "
Casts	"	.	.	40 " 11.6 "

Quartan fever—8 cases:

Albumin present in	.	.	.	4 cases.—50.0 per cent.
No albumin	"	.	.	4 " 50.0 "
Casts	"	.	.	3 " 37.5 "

Regularly intermittent fevers (tertian and quartan)—352 cases:

Albumin present in	.	.	.	136 cases.—38.6 per cent.
No albumin	"	.	.	216 " 61.3 "
Casts	"	.	.	43 " 12.2 "

Æstivo-autumnal fever—283 cases:

Albumin present in	.	.	.	165 cases.—58.3 per cent.
No albumin	"	.	.	118 " 41.6 "
Casts	"	.	.	70 " 24.7 "

Combined infection (tertian and æstivo-autumnal)—26 cases:

Albumin present in	.	.	.	11 cases.—42.3 per cent.
No albumin	"	.	.	15 " 57.6 "
Casts	"	.	.	7 " 26.9 "

Cases of uncertain type—30 cases:

Albumin present in	.	.	.	9 cases.—30.0 per cent.
No albumin	"	.	.	21 " 70.0 "
Casts	"	.	.	1 " 3.3 "

It thus becomes evident that albuminuria has occurred in nearly one-half of all the cases of malarial fever treated in the hospital. In the regularly intermittent fevers, tertian and quartan, the proportion of cases of albuminuria was 38.6 per cent., while in the æstivo-autumnal infections, the majority of all cases, 58.3 per cent., showed albumin in the urine. The large percentage in æstivo-autumnal fever is not remarkable when one considers the many other clinical evidences of the greater malignancy of infections with the æstivo-autumnal parasite.

Our statistics show, however, a rather strikingly large proportion of instances of albuminuria in all types. They can scarcely be compared to those of Anders, who has used the qualifying term "marked."

The percentage is, however, five times as large as that of Atkinson,¹ who found albuminuria in 9 per cent. of 121 cases.

Particularly conspicuous is the high percentage of albuminuria among the cases of aestivo-autumnal fever. It is in the more severe infections with this variety of parasites that the so-called remittent and pernicious fevers most commonly occur, and in these more severe attacks it would be but fair to assume that the percentage of cases showing albumin would be yet larger than that shown by our figures. And yet it is in just these cases that, at times, the question of a differential diagnosis between yellow fever and malarial fever is believed by some authors to hang upon the presence or absence of albumin in the urine.

It may be interesting to compare the frequency with which we have found albumin in the urine of patients with malarial fever with our own statistics and those of others with relation to certain other of the acute infectious diseases.

Typhoid Fever. Here we may use our own statistics. In 389 cases of typhoid fever from the statistics of Hewetson and Osler, albumin was observed in 303 instances, or 78 per cent., and casts in 164, or 42.2 per cent.²

Scarlet Fever. The frequency of albuminuria in scarlet fever has been variously estimated. Miller,³ Patrick,⁴ Steiner,⁵ and Guebler,⁶ as well as Lecorché and Talamon,⁷ believe that albuminuria is practically always present during the febrile period of the disease. Séé⁸ estimated that it was present in more than one-half the cases; Haidenheim in 80 per cent.⁹ Cadet de Gassicourt¹⁰ found albumin in 21 out of 65 cases, but believes these figures to be too high. Barthez and Sanné¹¹ believe it to be relatively rare, while Vogel¹² found it in two instances out of 50 or 60 cases, and Thompson¹³ in 40 out of 112 instances.

¹ Op. cit.

² Hewetson: Johns Hopkins Hospital Reports, 1894, iv. 113. Osler: Johns Hopkins Hospital Reports, 1895, v. 281.

³ Lancet, 1849, ii. 1, 57, 113, 197, 281, 524, 685.

⁴ Cited by Guinon: Art. "Scarlatine," in *Traité de Méd.*, Charcot, Bouchard, Brissaud, Svo, Paris, 1892, t. ii.

⁵ Compendium der Kinderkrankheiten, 3d ed., 8vo, Leipsic, 1878.

⁶ Dict. Encycl. des Sci. Méd., Par., 1869, ii. 476.

⁷ Cited by Guinon: Op. cit.

⁸ Le Moniteur des Hôp., 1858, 659.

⁹ Cited by Barthez and Sanné.

¹⁰ France Méd., Par., 1881, ii. 388, 400.

¹¹ Traité clin. et prat. des maladies des enfants. 3d ed., Par., 1891, 124.

¹² Cited by Barthez and Sanné.

¹³ Med.-Chir. Transactions, 1887.

The later albuminuria, that occurring during convalescence, was observed in 30 per cent. of the cases of Cadet de Gassicourt, and in 55 out of the 112 cases studied by Thompson.

Caiger,¹ in the London Fever Hospital, found albuminuria present in but 7.69 per cent. of 4015 cases; he asserts that the frequency of this condition is much less than is generally supposed. He omits, however, from his statistics those cases in which "but a faint and transient cloud of albumin was noted for less than three days."

My friend, Dr. McCollom, has very kindly sent me the results of the examination of the urine in 100 cases of scarlet fever in the Boston City Hospital:

½ to ¼ per cent. of albumin	4 cases.
¼ per cent. of albumin	1 case.
Large trace "	"	1 "
Trace "	"	4 cases.
Slight trace "	"	14 "
Very slight trace of albumin	15 "
Slightest possible trace of albumin	49 "
No albumin	12 "
						100 cases.

Diphtheria. The frequency of albuminuria in diphtheria is also variously estimated. Sée² believed it was present in one-third or a half of all cases. Maugin and Bergeron³ assert that it occurs in the majority of instances. Bouchut and Empis⁴ estimate its frequency at 66½ per cent., as does also Ebert.⁵ Smith⁶ found it present in 24 out of 62 cases, or 38.7 per cent., but believes that the proportion is probably greater, inasmuch as albumin was often missed, owing to the transient character of the symptoms. Sanné⁷ found albumin in 224 out of 400 cases, or 54.5 per cent. By far the most satisfactory statistics are those of McCollom.⁸ Out of 623 cases of diphtheria albumin was present in 57.7 per cent.

If we compare our statistics of malarial fever with those of *typhoid*

¹ Article "Scarlet Fever," in "A System of Medicine," etc., edited by T. Clifford Allbutt. London, 1897, vol. ii. 151.

² Op. cit.

³ Moniteur des Hôpitaux, Par., 1858, vi. 1035, 1043, 1051, 1064.

⁴ Gaz. des Hôp., 1858, 524.

⁵ Cited by Oertel, Ziemssen's Cyclopædia, Amer. edition, i. 603.

⁶ Keating's Cyclopædia of Diseases of Children, i. 626.

⁷ Traité de la diphthérie, 8^e, Par., 1877, pp. 128 et seq.

⁸ Med. and Surg. Reports, Boston City Hospital, 9th series, Boston, 1898, p. 27.

fever we find that malaria stands well behind the former affection in the frequency with which albuminuria is observed. The figures show:

Percentage of cases of albuminuria in malarial fever	46.4
" " " typhoid fever	78
" " in which tube casts were found in malarial fever	17.5
" " " " " typhoid fever	42.2

This is not remarkable when one considers through how long a period the kidneys of a patient with typhoid fever are subjected to the influence of the toxic products of the infection, as well as to the continued high temperature.

If, however, we compare the percentages in the more severe æstivo-autumnal fevers, the figures approach one another more closely:

Scarlet Fever. From a consideration of the varying estimates above mentioned it would appear that albumin is in all probability present in at least one-half the cases of scarlet fever. McCollom's figures indicate a still higher percentage. It is, perhaps, possible that in a certain proportion of the 49 per cent. of cases where the "slightest possible trace of albumin" was found this minute quantity would have passed unobserved with ordinary routine methods of urine examination.

It may, perhaps, be fair to compare Caiger's estimate, where those cases showing "a faint and transient cloud lasting less than three days" were omitted, with our cases in which casts were found. Such a table shows:

Caiger's statistics of the frequency of albuminuria in scarlet fever, 7.69 per cent.

Percentage of our cases of malarial fever in which albumin and casts were present, 17.5 per cent.

Despite these figures, and especially in view of McCollom's table, there can be little doubt that albuminuria is considerably more frequent in scarlet fever than in malaria.

Diphtheria. Assuming that McCollom's figures form a fair basis of comparison, we find:

Percentage of cases of albuminuria in malarial fever	46.4
" " " diphtheria	57.3

And this slight discrepancy in favor of diphtheria disappears when we consider æstivo-autumnal fever separately :

Percentage of cases of albuminuria in æstivo-autumnal fever	58.3
" " " diphtheria	57.3

Albuminuria, then, is more common in such notoriously severe acute infections as typhoid fever, scarlet fever, and diphtheria than in malaria; the difference, however, is by no means great. While occurring in only 38.6 per cent. of the regularly intermittent fevers, the frequency of albuminuria in æstivo-autumnal fever is probably fully as great as in diphtheria, and by no means so very much less than in typhoid and scarlet fevers.

Yellow Fever. While the occurrence of albumin in the urine in malarial fever cannot be compared in frequency with that observed in yellow fever, and while the amount, when present, is probably usually smaller, the fact that a majority of all instances of æstivo-autumnal fever in the climate of Baltimore, cases lasting but a short time and treated almost immediately by quinine, showed albuminuria, is strong presumptive evidence in favor of the idea that a considerably larger percentage of the severe pernicious cases which are most likely to be confounded with yellow fever must show this symptom. This would suggest caution in placing too great reliance upon the mere presence of albumin as evidence of the existence of yellow fever in a suspicious case.

It may be asked whether our figures represent the condition in the first days of an æstivo-autumnal infection. I think it may fairly be asserted that they do.

There were 96 cases of æstivo-autumnal fever in which the urine was examined within a week after the first symptoms of the infection. In the urine of these cases, albumin was present in 57, or 59.3 per cent., and casts were present in 28, or 29.1 per cent.

ACUTE NEPHRITIS.

Among 1832 cases of malarial fever occurring in the Johns Hopkins Hospital and Dispensary we have observed 26 instances of acute

nephritis. In 3 of these instances there is room for possible doubt as to whether the nephritis may not have preceded the malarial infection, though in none is this believed to have been the case. There were:

Instances of tertian fever	7
" æstivo-autumnal fever	16
" quartan fever	1
" combined infection (tertian and æstivo-autumnal)	1
" uncertain type	1
 Total	 26

These were all typical cases of acute nephritis, the majority showing oedema, while abundant albumin and numerous casts and usually blood-corpuscles and epithelium were found in the urine.

In 14 instances the complication occurred in the first attack of malaria; in 11 the patient had suffered from one or more previous infections; in 1 there was no history obtainable.

In 13 instances the complication ended in recovery (Cases III., IV., V., VII., IX., X., XI., XII., XIII., XVIII., XIX., XXII., XXIV.).¹

In 4 instances the complication ended in death (Cases I., II., XV., XVI.).

In 9 instances the result was doubtful (Cases VI., VIII., XIV., XVII., XX., XXI., XXIII., XXV., XXVI.).

Fatal Cases. The four fatal cases include the three instances in which some doubt may be held as to the true malarial nature of the case (Cases II., XV., XVI.).

In Case II. there was a history of oedema and bloody urine for several months, while regular chills had been noted but three weeks. The patient, however, had throughout this period been working in an extremely malarious district at the most dangerous time of the year. It is improbable that his malaria was acquired in December; far more likely that the infection occurred earlier in the season. He was a dull, stupid negro, and experience has shown us that a clear history of the time of onset of a malarial infection is often very difficult to obtain in such instances.

In Case XV. the clinical observation was unsatisfactory. Death

¹ In Cases III., IV., and V. there was still a trace of albumin present on discharge. In Cases XII. and XXIV., dispensary patients, but one examination of the urine is recorded. In all instances, however, the general condition warranted the conclusion that the patients were on the road to definite recovery.

occurred in coma, the breath having a urinous odor and the urine containing one-fourth per cent. of albumin; the illness apparently began sharply with a malarial infection two weeks before. The record of the examination of the urinary sediment, however, was incomplete.

Case XVI. was one of characteristic acute nephritis which took on a chronic course, resulting fatally seven months after the onset. The patient had been living in a malarious district, and had had chills and fever for a month and a half before entry, associated with anasarca, ascites, and evidences of acute nephritis. (Edema of the feet, however, was said to have been noticed for a month before the onset of the chills. In this case there is a history of scarlet fever (without dropsy) six years before. It is our belief, in view of the absence of other causes, that all three of these instances were true malarial nephritis. It is but fair, however, to point to the possibility that another view of the matter may be taken.

In Cases XV. and XVI. autopsy was not permitted.

Case I. was an instance of pernicious fever in which death was due to the acute infection rather than to the nephritis. In Cases I. and II. the anatomical changes have been excellently described by Dr. Barker.

HISTORIES OF FOUR FATAL CASES.

CASE I. Pernicious malarial fever; æstivo-autumnal infection; acute nephritis; death; autopsy.—No. 1769. J. B., male, aged thirty-four years, entered the hospital on September 10, 1890, complaining of fever, weakness, and headache. The patient has been sleeping on the ground in a very malarious district. For three days he has complained of great weakness and continuous vomiting. No further history is obtainable.

Physical examination. The patient is very weak and tremulous; tongue coated; thorax negative; spleen palpable; pulse 104; temperature 101°.

Blood. Æstivo-autumnal parasites; hyaline ameboid bodies in great numbers.

Sept. 11. The temperature rose this evening to 102°. No great change in the condition.

12th. The patient seems better to-day; vomiting is less frequent.

Treatment. Quinine, 0.325 (gr. v) three times a day.

On the 13th and 14th there was no vomiting, but the patient complained of great weakness. On the evening of the 15th the patient passed into a peculiar condition; he became drowsy and dull, and was aroused only with great difficulty; he was restless and uneasy, turning and tossing the clothes about; occasional vomiting. Throughout the night of the 15th the patient was restless and there was hiccup; the temperature, which had been nor-

mal since the 12th, fell to a subnormal point; the vomitus during the night was tinged with blood. On the morning of the 16th the patient was catheterized, 1500 c.c. of urine being obtained. The examination showed a specific gravity of 1010; a moderate quantity of albumin. The sediment contained many casts, chiefly granular and hyaline, though partly epithelial casts were not uncommon.

At 4 o'clock in the afternoon the temperature had fallen to 96°. The patient was very restless, cold, and dusky; growing steadily weaker and finally unconscious, he died at 8.45 P.M.

Autopsy. (Dr. Councilman.) Diagnosis: Pernicious malaria; acute splenic tumor; malarial pigmentation of spleen and liver; hypostatic congestion of the lungs. . . . The kidneys were large and swollen, surface mottled, capsules adherent in places. On section the consistency is firm, the Malpighian tufts are prominent and congested. The medullary rays are pale, and between them the lines of vessels are deeply reddened. No areas of opacity are visible. The cortex is distinctly, though slightly, pallid." . . .

Microscopical examination by Dr. Barker:¹ "On microscopical examination all the bloodvessels of the kidneys were found to be dilated, the veins of the pyramids being especially wide. There is irregular dilatation of the glomerular capillaries. Comparatively few parasites are present in the kidneys, although some distinct forms are visible within the veins and capillaries. A number of phagocytic cells can be seen, intravascular phagocytes and endothelial cells. The capsules of some of the glomeruli have undergone fibrous thickening. In places the capsular endothelium is proliferated. The endothelium of the convoluted tubules is swollen and granular, and there are numerous hyaline casts to be seen in the small collecting tubules. In the pyramids haemoglobin casts can be made out."

In this instance the nephritis, as in most cases of typhoid fever, played but a small part in the clinical picture of the disease. Possibly, had the patient recovered from the acute infection, or had life been further prolonged, clinical evidence of the renal changes might have appeared.

CASE II. Malarial fever; double tertian infection; subacute nephritis; death three and a half months after onset.—No. 5421. L. W., male, colored, aged twenty-three years; admitted January 9, 1893. Family and personal history negative. Gonorrhœa nine years ago. Three months ago, while working in a very malarious district, began to suffer from frequent micturition, general oedema, and bloody urine. For three weeks has had regular tertian chills.

Physical examination. Marked general oedema; ascites; no cardiac hypertrophy; pulse tension not increased; spleen not palpable (distended abdomen).

¹ Johns Hopkins Hospital Reports, 1895, v. 284.

Blood. The blood was not examined until after death; it then showed an extremely severe double tertian infection.

Urine. Dark amber; clear; acid; 1017; large amount of albumin. Sediment; hyaline, granular, and epithelial casts; many epithelial cells. There were daily febrile paroxysms, the nature of which was not appreciated during life. The urine ranged in quantity at first between 500 and 1000 c.c., diminishing gradually before death. For the last three days it amounted to but 260 to 350 c.c. The patient became enormously oedematous, and grew more and more anaemic. He was dull and stupid, but restless and uneasy. On January 26, 1893, he died.

The patient was treated throughout as a case of nephritis. A milk diet was ordered and frequent hot baths. Diuretin and digitalis were given internally.

Autopsy. (Dr. Councilman.) "Anatomical diagnosis: Acute malarial fever; double tertian infection; general streptococcus infection; subacute Bright's disease; malarial pigmentation of the organs; chronic passive congestion; general anasarca; infarctions of kidneys; erysipelas." . . ."

"*The Blood.* Examined fresh from the peripheral veins and various internal organs showed enormous numbers of malarial parasites, most of them nearly full-grown; others only half-grown (tertian type), many of them enclosed within the protoplasm of large mononuclear leucocytes. . . ."

"The kidneys together weigh 400 grammes. They are both alike in size and general appearance. On the surfaces of each a few small fresh infarctions with hemorrhagic margins are visible. The capsules strip off easily. The general color of the external surfaces of the kidneys beneath the capsules is yellowish-brown, marked by scattered opaque darker areas, and here and there by minute hemorrhages. The whole kidney has a rather soft, oedematous feel. On section, the cortex has a yellowish appearance and is rather translucent; pyramids reddened, contrasting sharply with the lighter-colored cortex. In some parts of the cortex the striae are well marked, in others they are less apparent or invisible. Average width of cortex 1 cm. A small amount of fluid exudes from the cortical substance on pressure. The glomeruli are indistinct. . . . Frozen sections of the *kidney* show a very little fat in fine droplets in the glomeruli. The epithelial cells of the tubules in the labyrinth are much swollen and are filled with fine albuminous granules and hyaline droplets. Many of the tubules are dilated and are lined by low epithelium. Casts are numerous in sections, and in urine collected from the bladder. Coagulated albumin is visible in the capsular spaces, in frozen sections made from a bit of kidney previously fixed in boiling water. The capsular epithelium is swollen and evidently proliferated. . . ."

The kidneys were carefully studied by Dr. Barker.¹

"*The Kidney.* An examination of many glomeruli shows considerable variation in the size of the capsular spaces. While in some instances the glomerulus almost completely fills out Bowman's capsule, the space being a mere

¹ Johns Hopkins Hospital Reports, vol. v. p. 257.

chink, in others the latter is equal in size to one-third of the whole capsule. The space is not always empty, but may contain coagulated albumin, red blood-corpuses and shadows, or a few mononuclear cells (desquamated epithelium). The fibrous capsules are not thickened except occasionally, where an atrophied glomerulus is visible. Frequently just outside the capsule of Bowman a narrow clear space can be made out, and this may contain a few cells, chiefly polynuclear leucocytes, or even be crowded with them. In many of the capsules the capsular epithelium is evidently proliferated, the whole inside of the space being lined by nuclei with intensely staining chromatin. The glomerular capillaries vary in their size and contents; some of them are empty, others are distended. Occasionally one is seen to be plugged with streptococci. The number of white corpuscles within the glomerular capillaries also varies; they are very irregularly distributed; in some glomeruli scarcely any are present; in others, one, two, or more of the glomerular capillaries may be packed full of polynuclear leucocytes. In a section stained in methylene-blue a capillary is visible plugged at one point with streptococci and crowded throughout the rest of its extent with leucocytes, with polymorphous nuclei—reminding one forcibly of the appearance of the capillary glass tubes in an experiment in positive chemotaxis. On the other hand, masses of cocci may be seen with no neighboring leucocytic accumulation. The nuclei of the polynuclear leucocytes vary in appearance: some stain sharply, and take on the ordinary forms; others stain less sharply, have a blurred look, and assume bizarre shapes. The protoplasm of the polynuclear leucocytes frequently contains granules or minute clumps of granules of malarial pigment, occasionally a well-formed parasite or short chains of cocci. There is some malarial pigment in the glomeruli contained within the protoplasm of mononuclear cells. The majority of the malarial parasites in the glomerular capillaries are outside nucleated cells. Here and there in specimens stained with aqueous magenta a giant spindle shaped nucleus is visible. The lumina of the convoluted tubules are for the most part wide, and are lined with rather low cubical epithelium. There are a few areas of dilated tubules in which the lining epithelium is flattened so as to resemble endothelium. The nuclei of the epithelial cells, as a rule, stain normally, although in some swollen cells they stain feebly, and in some tubules the nuclei are shrunken and the chromatin stains more intensely than normally.

Many of the convoluted tubules and collecting tubules contain hyaline casts; and hyaline droplets are visible within the swollen lining epithelial cells. These droplets, both the finer and the coarser, and the upper portions of the hyaline casts, stain intensely in Weigert's fibrin stain. Occasionally desquamated epithelial cells and a few red blood-corpuses and round yellowish striped urinary concrements are to be seen within the lumina of the tubes.

The intertubular capillaries contain enormous numbers of streptococci (methylene-blue, Weigert's fibrin stain). Many of them are dilated and completely plugged with cocci, and sometimes chains of cocci are visible in

narrow pericapillary spaces. As in the glomerular vessels, some of the intertubular capillaries are crowded with leucocytes. Some of the small veins in the cortex are actually thrombosed with masses of streptococci, large numbers of malarial parasites, white corpuscles (some of which are necrotic), and pigment clumps. No bacteria other than streptococci are present anywhere in the kidney.

In the interstitial tissue of the kidney there is a slight but evident increase in the number of the cells of the lymphoid type. There are small nodal masses of smaller and larger round cells, usually with but little perinuclear protoplasm, many of them with fragmented nuclei. These minute nodes may contain, besides lymphoid cells, single polynuclear leucocytes or epithelioid cells.

Sections of the kidney treated with ferrocyanide of potassium and hydrochloric acid show an almost entire absence of cells containing haemosiderin. Here and there, however, a little is visible within the protoplasm of the endothelium of the vessels.

The infarcted areas of the kidney present the lesions ordinarily seen under these circumstances—anaemic necrosis and neighboring reaction. The whole of the necrotic areas—glomeruli, tubules, bloodvessels, interstitial tissue—refuses to stain in the ordinary nuclear dyes, and has an increased affinity for eosin. The only nuclei which stain are those of polynuclear leucocytes which have invaded the interstitial tissue everywhere, and are accumulated in large numbers at the margins of the infarcted areas, and in the neighboring dilated bloodvessels. There is extensive nuclear fragmentation in these polynuclear leucocytes, and the most varied distortion-processes (*abschnürrungsvorgänge*) of their nuclei are visible. Many of the bloodvessels at the apices and in the peripheries of these infarctions are thrombosed with streptococci, enormous numbers of malarial organisms, over 100 of which were counted inside the lumen of one vessel, and white cells. Small bits of the kidney hardened in Flemming's stronger solution and stained with aqueous magenta yield very instructive sections. Fine fat droplets are visible in the glomeruli and in the epithelium lining the capsular spaces. The convoluted tubules are not extensively fatty; some are entirely free from fat droplets, others show numerous smaller and larger droplets, especially at the proximal ends of the lining epithelial cells. Fine fat droplets are also visible in the protoplasm of some of the leucocytes in the vessels, and also in the smooth muscle fibres of the arteries. The desquamated epithelial cells within the lumina of the tubules contain numerous rather coarse fat droplets. The cells of the convoluted tubules in sections prepared in this way are seen to be finely granular, and the hyaline degeneration of the protoplasm is well shown. Many of them contain large vacuole-like spaces which sometimes displace the nuclei. In some of the tubes free red blood-corpuscles, polynuclear leucocytes, and malarial organisms are visible. The last named are sometimes free or lie on red blood-corpuscles; sometimes they are enclosed within cells. They are to be seen in both polynuclear and mononuclear cells

within the lumen of the convoluted tubules. In one tubule, besides numerous red blood-corpuses and shadows, four free well-formed malarial organisms and a mononuclear cell containing within its protoplasm five malarial organisms of the same stage of development can be made out. Pictures such as these were seen too often to be accounted for by technical accidents. Occasionally red corpuscles, malarial parasites, and white cells are visible within the glomerular capsular spaces.

The time at which the streptococcus infection came on is not clear.

CASE XV. Malarial fever; tertian infection; nephritis; uræmia; coma: death; no autopsy.—No. 17,406. P. J., female, aged fourteen years; admitted September 26, 1896. The patient had chills and fever during six months last year. No history of other infectious diseases. Eleven days ago she began to suffer from pains in neck and legs, dyspnea on exertion, fever, and cold sensations.

Physical examination. The face has a pasty white color; lips pale; tongue coated. The patient is very apathetic; somewhat delirious; spleen not palpable; no œdema; breath has a urinous odor.

Blood. Extra-cellular tertian bodies. Leucocytosis of 21,000.

Urine. Passed involuntarily, and lost.

Temperature. Subnormal.

On the 27th the patient became comatose.

Urine. Catheterized specimen: pale yellow; opaque; 1008; albumin + per cent. The sediment contains considerable pus. No casts or blood to be seen.

Despite hypodermatic injections of quinine and stimulation, the patient died comatose on the 27th. Autopsy was not allowed.

This case is unsatisfactorily recorded. The author was absent at the time, but Dr. Camac, who saw the case, tells me that there is little doubt that the death was from uræmia.

As to the causal influence of the malaria there must be some question.

CASE XVI. Malarial fever; astivo-autumnal infection; acute nephritis, becoming chronic; death.—No. 17,621. I. A., female, aged fourteen years, entered October 17, 1896. Family history negative. The patient had measles and whooping-cough as a child; scarlet fever six years ago. Has always been well and strong. She lives in a most malarious district. Two and a half months ago she began to notice slight œdema of feet and puffiness of eyes. A month and a half ago began to have chills and fever. At this time the swelling increased considerably, involving the genitalia and abdomen, and becoming very troublesome. The urine was reduced in quantity and red. There was marked pallor. The chills disappeared under treatment; she had but seven or eight in all, and thinks she has quite recovered from the malaria.

Physical examination. Marked pallor; general œdema and ascites. Heart's apex in fourth space, eight cm. from median line. Second aortic sound markedly accentuated.

Blood. Half-grown tertian parasites.

Urine. Pale; acid; 1012; albumin one-half per cent.; sediment abundant; epithelial cells, small round, and larger flat; hyaline, finely and coarsely granular casts; blood casts; pus cells; granular matter.

Under quinine the parasites rapidly disappeared. The temperature was normal. The urine, however, was always reduced in quantity and the œdema never cleared up. The pulse throughout was of high tension; second aortic sound markedly accentuated. Uræmic symptoms—headache, vomiting, and eventually coma—existed for five months, death occurring on March 20th. The albumin at times was present in as large quantities as 0.7 per cent. The patient was kept for the greater part of the time on a milk-diet; various diuretics and iron were given internally; hot-water and hot-air baths, with pilocarpine hypodermically, were given with only temporary effect. No autopsy was permitted.

Cases with uncertain result.

In nine instances (Cases VI., VIII., XIV., XVII., XX., XXI., XXIII., XXV., and XXVI.) the final outcome of the nephritis is not perfectly clear, though in the majority recovery probably occurred.

Cases XXIII., XXV., and XXVI. were observed in the dispensary, and were seen on but one occasion.

Case VI. was an instance of mild acute hemorrhagic nephritis occurring in aestivo-autumnal fever. The patient left a week after admission, feeling perfectly well, the urine, however, containing at the time of discharge a trace of albumin, while the sediment showed occasional hyaline and granular casts and red blood-corpuses. There was no cardiac hypertrophy, no increase in the blood tension; never any œdema.

Case XIV. was that of a man, aged forty-one years, who had suffered off and on for a month with daily chills and for ten days with œdema of the face and extremities. The urine showed the characteristics of a mild acute hemorrhagic nephritis. Considerable improvement in the general condition occurred under quinine, but the patient had a carbuncle upon the back of the neck, and four days after entry left the hospital against advice, dreading an advised operation.

In Cases XVII., XX., and XXI., especially in the two former, there is some possibility that the process may have become chronic. These cases will be considered later.

GENERAL ANALYSIS OF 26 CASES OF ACUTE MALARIAL NEPHRITIS.

<i>Age:</i> From 1-10 years	2 cases.
“ 10-20 “	4 “
“ 20-30 “	9 “
“ 30-40 “	6 “
“ 40-50 “	5 “
Total	26 cases.

The figures in this table run practically parallel to those in our former statistics as to the relative frequency of malarial fever, with the exception of the slightly greater percentage of cases of nephritis between the ages of forty and fifty. The small percentage of cases under ten years of age is perhaps explained by the absence of a children's ward in the hospital.

Sex: Of the 26 cases there were: Males, 17 (65.3 per cent.); females 9 (34.6 per cent.).

Race: 20 of the 26 cases were in white patients (76.9 per cent.) and 6 in negroes (23 per cent.).

These latter figures are striking. Of 1832 cases of malarial fever but 82 (4.4 per cent.) were in colored patients; and yet of these few patients 6 (7.3 per cent.) developed acute nephritis, against 20 (1.1 per cent.) in 1750 whites.

These figures are quite in keeping with the clinical fact which we have learned to recognize, in this hospital at least—namely, that the colored race is more susceptible to renal disease than the white.

Relation of the Time of Development of the Nephritis to the Season of the Year.

TABLE SHOWING THE TIME OF DEVELOPMENT OF 26 CASES.

January	.	.	.	0	July	.	.	.	5
February	.	.	.	0	August	.	.	.	5
March	.	.	.	1	September	.	.	.	7
April	.	.	.	1	October	.	.	.	6
May	.	.	.	0	November	.	.	.	0
June	.	.	.	1	December	.	.	.	0—26.

It would thus appear that nephritis is much commoner at the height of the malarial season; rare in the early months of the year. Of these cases 11.5 per cent. only developed before July, while our statistics in

1712 cases as to the time of onset of the symptoms of malarial infection show that 17.1 per cent. develop during this period. The greater relative frequency of malarial nephritis in the second half year is clearly explained by its predominance in æstivo-autumnal fever.

Edema was present in 19 of the 26 cases.

Blood was noted in the urine in 18 cases; it was absent in 7, while in 1 instance no note upon the sediment was made.

An exact estimate as to the *relative frequency* of nephritis in malaria is difficult to make. If we take into consideration the entire 1832 cases, it must be remembered that the urine was examined in the out-patient department in rare instances only, when the attention of the physician was definitely called to the possibility of some renal complication. And it is quite possible that cases of true nephritis may, under these circumstances, have escaped observation.

Among these 1832 instances of malarial fever there were 26 cases of acute nephritis, or 1.4 per cent.

The following table will show the *percentage of renal complications in the different types of fever*:

Regularly intermittent fevers

(tertian and quartan) . . .	1014 cases	—nephritis, 8 cases	0.78 per cent.
Æstivo-autumnal fever . . .	676 "	" 16 "	2.3 "
Combined infections . . .	36 "	" 1 "	0.9 "

A more accurate estimate of the frequency of nephritis in malaria is probably to be obtained by a study of the cases observed within the hospital—758 in number. The objection might be raised that these cases were, as a rule, somewhat more severe than those observed in the dispensary. But, inasmuch as all patients presenting themselves at the dispensary with malaria are recommended for admission, many of the mildest cases entering, this objection is probably not as important as it might appear at first. It is probably safe to say that the figures obtained from the house-cases, while doubtless somewhat too high, are less out of the way than those obtained from a consideration of the total number.

Among the 758 cases of malarial fever treated in the Johns Hopkins Hospital there were 21 instances of acute nephritis of probably malarial origin, or, in other words, 2.7 per cent. In three of these instances there is room for some doubt as to whether, possibly, the

infection may not have occurred after the beginning of the nephritis. Leaving out these possible doubtful cases, we are then left with a percentage of 2.3 of acute nephritis.

The frequency of acute nephritis in æstivo-autumnal fever was, as might have been expected, far greater than in the regularly intermittent fevers.

In 394 cases of tertian and quartan fever there were 6 instances of nephritis (1.5 per cent.), or, if we omit the 3 cases in which there is some doubt as to the etiology of the nephritis, 3 instances (0.7 per cent.).

Among 296 cases of æstivo-autumnal fever there were 14 instances of acute nephritis (4.7 per cent.).

Out of 26 instances of combined infections there was 1 case of acute nephritis (3.5 per cent.).

A comparison of these statistics with those of other observers in other acute infections is interesting.

a. *Typhoid Fever.* Among 389 cases of typhoid fever we have had 14 instances of acute nephritis,¹ or 3.6 per cent. In none of these cases, however, was œdema present, and in none of the fatal cases was death apparently due to the renal complication. Complete recovery occurred in all instances which did not die from other complications of typhoid fever.

b. *Scarlet Fever.* The most satisfactory statistics are those of Caiger,² who observed, among 4015 cases of scarlet fever in the London Fever Hospital, 3.31 per cent. of instances of acute nephritis, a percentage but little higher than that observed by us in all varieties of malaria—2.7 per cent.

c. *Diphtheria.* In diphtheria the frequency of true acute nephritis is difficult to estimate.

Trousseaur³ observed dropsies in barely 5 per cent. of his cases; Sanné,⁴ in 7 (3.1 per cent.) out of 224 instances in which albuminuria was present, or in 1.7 per cent. of all his cases. In our cases of

¹ The determination of what shall be called clinically "acute nephritis" is necessarily somewhat arbitrary. Among our cases, in the absence of gross clinical evidence of renal disturbance, we have included only those where the urine showed a large quantity of albumin with numerous casts—or, if the albumin were not especially abundant, where the sediment showed, in addition to casts, blood and renal epithelium. We have, for this reason, omitted from our typhoid statistics some of the cases classed by Hewetson as nephritis.

² Op. cit.

³ Quoted from Barthez and Sanné, op. cit., p. 457.

⁴ *Traité de la diphthérie*, 8vo, Par., 1877.

malaria, dropsy was present in 4.6 per cent. of the cases in which there was albuminuria, or in 1.9 per cent. of all our cases.

From McCollom's valuable statistics nephritis would appear to be an unimportant complication of diphtheria. But 5.2 per cent. of 633 cases had over 0.1 per cent. albumin in the urine, while oedema was noticed in but 4 instances. "In the 71 autopsies, in no instance was the condition of the kidneys such as to have materially contributed to the fatal issue."

It may then be seen that while albuminuria is more common in typhoid fever than in malaria, true acute nephritis, with general dropsy and other characteristic symptoms, is apparently of greater frequency in the latter affection. And while malarial fever cannot be said to exercise as deleterious an influence upon the kidneys as does scarlet fever, the percentage of acute nephritis among our cases of malaria is more than half as large as that of Caiger in scarlet fever.

Considering the different types of malarial affection separately, these facts are more strikingly brought forth. The percentage of cases of acute nephritis in our 296 instances of æstivo-autumnal fever is higher than that in any of the above-mentioned infections.

TABLE.

Percentage of cases of nephritis in æstivo-autumnal fever	4.7
" " " typhoid fever	3.6
" " " scarlet fever (Caiger)	3.5

In comparison to Sanné's estimate that 3.1 per cent. of the albuminurias in diphtheria have dropsy, we have the fact that out of 165 cases of albuminuria in æstivo-autumnal fever 9, or 5.4 per cent., showed this symptom.

In view of these figures it is difficult to escape the conclusion that malarial fever is one of the acute infections in which acute nephritis is comparatively common. This is especially true of æstivo-autumnal infections where its frequency, if not its severity, would, from our statistics, appear to be equal to that of scarlet fever, typhoid fever, or diphtheria.

The important rôle which malarial fever plays in the etiology of acute nephritis in Baltimore is testified to by the fact that out of 112 instances of acute nephritis observed in the Johns Hopkins Hospital 21, or 18.7 per cent., were of malarial origin.

All observers agree that there is a great difference in the malign-

nancy of different infections, and our statistics would lead us to recognize the justice of this observation. Fifteen of our 26 instances of malarial fever occurred during the summer and fall of 1896, at a time when an unusually large amount of severe malarial fever prevailed.

It is not improbable that the especial malignancy of this epidemic of 1896 may account for the rather strikingly high percentage of instances of nephritis which have come under our observation.

Our statistics would lead us to assume that this complication is more frequent than it would appear to be in Rome from the observations of Rem-Picci.

CHRONIC NEPHRITIS.

What influence, if any, may malarial fever have upon the development of chronic nephritis?

In four instances of acute nephritis observed in the hospital there is some reason to believe that the process may have assumed a chronic course. The first (Case XVI.) has already been mentioned among the fatal cases (page 18). The patient died, after an illness lasting from six to seven months, with the symptoms of a chronic diffuse nephritis. An autopsy was not permitted. It will be remembered that there was some question in this case as to whether the malaria might not have been a secondary infection developing in a patient already suffering from nephritis. The time of onset of the trouble, the surroundings of the patient, the absence of other etiological elements, make it highly probable that the malarial infection was the primary cause of the disease.

CASE XVII. Malarial fever; double tertian infection; chronic nephritis; little improvement.—No. 17,836. A. T., female, colored, aged twenty-one years. Admitted November 10, 1896. Family and personal history good; no history of other infectious diseases. The patient suffered in September with chills and fever, which disappeared after treatment with quinine for one week, when she believed that she had completely recovered from the infection. For four weeks she has suffered with oedema of the back and legs, abdominal pain, headaches, cough, and dyspnoea. Two days ago had a chill.

Physical examination. Marked pallor; general oedema and ascites; right hydrothorax.

Heart. Apex in fifth space 12½ cm. from the median line; no accentuation of the second aortic sound. Spleen not palpable.

Blood. Tertian parasites.

Urine. Smoky; 1025; acid; albumin abundant, nearly 1 per cent. Sediment abundant; leucocytes; vaginal epithelial cells; occasional decolorized

red blood-corpuses; numerous hyaline and finely granular casts; some coarsely granular casts, many having small round cells adherent; occasional blood and epithelial casts.

There were slight febrile paroxysms on the 10th and 11th. Under treatment with quinine the temperature became normal on the 13th, and remained so thereafter.

The patient was placed on a milk diet, given diuretics (diuretin, bitartrate of potassium) and iron (Blaud's pills). Frequent hot baths, with and without the addition of pilocarpine hypodermatically, were given to induce sweating.

The urine, reduced in amount for the first several days, was normal or slightly increased in quantity thereafter. The specific gravity varied between 1025 on entrance and 1008 on December 2d. For the three weeks before discharge it averaged about 1010. The blood disappeared from the urine by the 18th of November, but returned again on the 21st. On the 5th of December the patient left against advice, still oedematous, the urine showing $\frac{1}{2}$ per cent. albumin.

In this instance the duration of the case (two and a half months); the persistence of the symptoms, and the continued large quantity of albumin, led us to believe that we were dealing with a chronic diffuse nephritis. Unfortunately, we have been unable to learn the subsequent history of the case.

CASE XX. Malarial fever; æstivo-autumnal infection; acute hemorrhagic nephritis; recovery (?).—No. 20,905. C. B., colored, aged twenty years. Admitted October 12, 1897. Family history negative. Measles, whooping-cough, and chicken-pox as a child. The patient has suffered for a month with daily and tertian chills. He has been taking quinine, and has had no chills for five days. Two weeks ago oedema of the legs and feet appeared, and a week later became general. The urine has been of a dark color.

Physical examination. Pallor; general anasarca; point of maximum cardiac impulse in the fourth space 10 cm. from the median line; pulse of rather high tension; spleen not palpable.

Blood. Æstivo-autumnal parasites, pigmented ovoid forms.

Urine. Yellow; acid; 1017; albumin 0.4 per cent.; sediment; many uric acid crystals; many granular, hyaline, and epithelial casts.

There were slight daily febrile paroxysms from the 15th to the 20th, on which date treatment with quinine, 0.325 (gr. v) every four hours was begun; the temperature reached normal by the 23d.

The patient was given a milk diet and bitartrate of potassium as a diuretic. Later, iron in the form of Blaud's pills was given.

On the 23d the urine suddenly became smoky, containing red blood-corpuses; it was somewhat reduced in quantity from the 23d to the 30th, after which time it was steadily above the normal amount, sometimes passing 3000 c.c. The albumin gradually diminished in quantity. The oedema and ascites had disappeared by the 26th. There was no evidence of albuminuric retinitis. There was no cardiac hypertrophy, the point of maximum impulse being in the fifth space 8.8 cm. from the median line just before discharge. A slight trace of albumin, however, still remained present in the urine.

On the 23d the patient left the hospital with a trace of albumin yet in the urine, and a few hyaline, granular, epithelial, and blood casts still present.

The patient has been heard from repeatedly since his departure. He believes himself to be well. A specimen of *urine* obtained several weeks ago (April 18, 1898) had a specific gravity of 1018. There was a very faint trace of albumin. Microscopically, a few red blood-corpuses were found in a centrifugalized specimen as well as one or two coarsely granular casts. From the patient's letter there would appear to have been a moderate polyuria.

CASE XXI. Malarial fever; æstivo-autumnal infection; acute hemorrhagic nephritis; recovery (?).—No. 20,981. C. K., male, aged thirty-one years. Admitted October 20, 1897. Family history negative. Had measles as a child and diphtheria (?) at thirteen. For twenty days the patient has had quotidian chills and fever, off and on, relieved at times by quinine. Two days ago the legs became œdematosus, and there was dyspnoea on exertion. The urine was of a reddish color.

Physical examination. Pallor; general anasarca; no cardiac hypertrophy; spleen not palpable.

Blood. Æstivo-autumnal parasites; hyaline amoeboid bodies.

Urine. Reddish brown; smoky; 1015; acid; albumin 0.4 per cent.; sediment abundant; numerous hyaline, epithelial, granular, and blood casts; red blood-corpuses, normal and decolorized; epithelial cells.

There was irregular fever for forty-eight hours.

Treatment with quinine was begun on the 21st, and the temperature was normal by the 23d. The patient was given a milk diet and bitartrate of potassium as a diuretic. Later, tr. ferri chloridi, 1 3 (mxx) t. i. d., was also given. The œdema slowly disappeared, remaining absent after November 15th.

The *urine*, only 700 c.c. in amount on October 21st, and 1290 on 22d, was afterward continually increased in quantity, the amount at times passing 2500 c.c. The albumin diminished rapidly, but was still present as a trace on discharge. No blood appeared in the sediment after December 24th.

The pulse tension was rather high, and the second aortic sound was somewhat accentuated, but no retinal changes were to be made out.

The patient was discharged at his own request on January 24, 1898, feeling quite well. The *urine* on this date was clear, acid, 1010. There was a trace of albumin. The sediment still showed a few granular casts.

In both of these instances there is some question as to whether or not the renal changes have assumed a chronic course. In Case XX. the presence of blood and an occasional cast in the urine six months after the onset of the affection, testifies to the gravity of the lesions produced by the acute infection while in Case XXI. the high blood tension and the persistence of albumin and casts were suspicious of a chronic change.

Case XVII. represented, apparently, a true chronic malarial nephritis, and, in view of the literature above quoted, there can be but

little doubt as to the existence of such cases. Although unable to present any further instances than these mentioned in support of such a view, it is, I think, safe to assume that any infection, the toxicity of which is sufficient to produce as large a percentage of serious acute nephritides as malarial fever, must play a certain part in the etiology of chronic renal changes.

It may probably be considered as a generally recognized fact that scarlet fever, diphtheria, and typhoid fever result sometimes in changes in the kidneys which may lead secondarily to grave chronic nephritis. And such changes are generally supposed to be due to circulating toxic substances, produced either directly by the growth of the infectious organisms, as in diphtheria, or set free from the bodies of the dead bacteria, as in typhoid fever, or resulting secondarily from the action of such substances on the fluids and tissues of the body.

The surprising frequency of acute nephritis in our cases of malarial fever would appear to be an indication of the extreme toxicity of the circulating poisons present, evidence of the existence of which has been previously brought forward in the grave changes noted by Guarneri,¹ Bignami,² Barker,³ Monti,⁴ and others in the spleen, liver, and brain. Does it not, perhaps, justify us in considering seriously whether, after all, repeated and chronic malarial infections may not play a greater part in the development of chronic renal changes than we have previously been in the habit of assuming?

SUMMARY.

In 758 cases of malarial fever treated in the wards of the Johns Hopkins Hospital albuminuria occurred in 46.4 per cent. and casts of the urinary tubules in 17.5 per cent.

Albuminuria was much more frequent in æstivo-autumnal fever than in the regularly intermittent fevers, occurring in but 38.6 per cent. of the latter and in 58.3 per cent. of the former, while casts of the renal tubules were found in 12.2 per cent. of tertian and quartan infections and in 24.7 per cent. of the cases of æstivo-autumnal fever.

The frequency of albuminuria in æstivo-autumnal fever is apparently equal to that in diphtheria, though less than in scarlet and typhoid fevers.

Out of 1832 cases of malarial fever in the hospital and in the out-

¹ Atti d. R. acc. med. di Roma, 1897, s. ii., iii., 247.

² Ibid., Anno xvi., 1890, s. ii., v. 317.

³ Johns Hopkins Hospital Reports, 1895, v. 220.

⁴ Bull. d. Soc. med.-chir. d. Pavia, 1895.

patient department there were 26 instances of nephritis of malarial origin, or 1.7 per cent. Of these, 13 recovered, 4 died, and in 9 the result was doubtful, 3 instances probably becoming chronic. In 3 of the fatal cases there is possible doubt as to the malarial nature of the case.

Nephritis occurs apparently in from 1 to 2 per cent. of all cases of malarial fever in the neighborhood of Baltimore. The complication is more frequent and severe in æstivo-autumnal fever; it is commonest during the height of the malarial season, in July, August, September, and October; it is rare in the first half of the year.

The relative frequency of malarial nephritis appears to be much greater in the negro than in the white race.

There is nothing especially distinctive in the clinical characters of the disease. It shows the usual features of an acute toxic nephritis; the tendency is apparently toward a short course and a favorable issue. Severe fatal or chronic forms of the disease may, however, occur, two, possibly four, instances of chronic nephritis of malarial origin having come under our observation.

CONCLUSIONS.

1. Albuminuria is a frequent occurrence in the malarial fevers of Baltimore, occurring in 46.4 per cent. of our cases.

2. It is considerably more frequent in æstivo-autumnal infections, occurring in 58.3 per cent. of these instances, against 38.6 per cent. in the regularly intermittent fevers.

3. Acute nephritis is a not unusual complication of malarial fever, having occurred in over two per cent. of the cases treated in the wards of the Johns Hopkins Hospital, and in between one and two per cent. of all cases seen at the institution.

4. The frequency of acute nephritis in æstivo-autumnal fever is much greater than in the regularly intermittent fevers, having been observed in 4.7 per cent. of the cases treated in our wards, and in 2.3 per cent. of all the cases seen.

5. The frequency of albuminuria and nephritis in malarial fever, while somewhat below that observed in the more severe acute infections, such as typhoid fever, scarlet fever, and diphtheria, is yet considerable.

6. There is reason to believe that malarial infection, especially in the more tropical countries, may play an appreciable part in the etiology of chronic renal disease.

CASES.

CASE I.—*Vide* page 13.

CASE II.—*Vide* page 14.

CASE III. *Estivo-autumnal malaria; acute hemorrhagic nephritis; recovery.*

—No. 8126. L. S., aged thirty-one years, was admitted September 6, 1893. Family history negative; had measles as a child. The patient lives in a very malarious district, and had chills and fever three years ago. A week before entry began to complain of œdema of the legs, dyspnoea, and cough with tenacious mucous expectoration.

Physical examination. Marked pallor; moderate œdema of the legs; fine moist râles at the bases of both lungs; no cardiac hypertrophy; pulse of normal tension; spleen palpable.

Blood. Estivo-autumnal parasites; hyaline amœboid bodies and crescents.

Urine. Dark reddish-brown; opaque; acid; 1021; much albumin. Sediment: very numerous hyaline, granular, epithelial, and blood-casts; red blood-corpuses, normal and decolorized; leucocytes; epithelial cells.

There were paroxysms of fever on the afternoons of the 7th and 8th; the fever rapidly disappeared under quinine, which was begun upon the 8th. On the 9th and 10th the patient was given four doses of quin. et ureæ muriatis, 0.65 (gr. x), hypodermatically. The albumin, at first nearly $\frac{1}{2}$ per cent., rapidly diminished to a faint trace on October 18th. No casts were to be found in the sediment after September 30th. The quantity of urine, at first diminished, was always above the normal after September 14th. On October 23d the patient was discharged, feeling perfectly well; the urine, however, still showed a faint trace of albumin. Beyond the quinine, which was administered in doses of 0.325 (gr. v) every four hours from September 9th to 23d, and afterward in doses of 0.325 (gr. v) three times a day, the patient received no medicinal treatment.

CASE IV. *Malarial fever; mixed estivo-autumnal and tertian infection; acute nephritis; recovery (?).*—No. 8302. J. J., aged thirty years, was admitted October 2, 1893. Family history negative; always healthy, except for an attack of malaria two years ago. For two weeks daily chills, headache, vomiting; for two days œdema of the hands and feet and vertigo.

Physical examination. Sallow color; marked pallor; moderate general œdema; arteries slightly thickened; no cardiac hypertrophy; no accentuation of second aortic sound; spleen palpable.

Blood. Mixed infection; estivo-autumnal and tertian parasites, the former in excess.

Urine. Reddish-amber; clear; acid; 1022; distinct trace of albumin. Sediment: granular and epithelial casts, many cylindroids, few leucocytes.

There were paroxysms of fever on the 2d, 3d, and 4th.

Treatment. Quinine 0.65 (gr. x) every four hours on the 2d, 3d, and 4th, and 0.325 three times a day from the 10th on.

The temperature, which had shown daily elevations, was normal after October 4, 1893. October 6th. Urine: dark-yellow; acid; 1015; trace of

albumin; many large epithelial and hyaline casts, some with blood adherent; few red blood-corpuscles; few leucocytes. The patient was discharged, apparently well, on the 12th. There was no final note upon the urine.

CASE V. Estivo-autumnal infection; acute hemorrhagic nephritis; possible exacerbation of a chronic nephritis; recovery (?).—No. 8558. F. L., male, aged thirty-eight years, was admitted November 4, 1893. Family history negative; measles as a child; typhoid fever fourteen years ago; smallpox eight months ago. Has had tertian chills off and on for four weeks, relieved occasionally by quinine. For two weeks there have been œdema of the feet and legs, dyspnoea, headache, frequent micturition, and ischuria.

Physical examination. Pallor; marked œdema of the legs; breath urinous; heart slightly hypertrophied; apex impulse in the sixth space just outside the mamillary line; second aortic sound accentuated; radial tension somewhat increased; artery not thickened; spleen palpable.

Blood. Estivo-autumnal parasites; hyaline, amorphous bodies, and crescents.

Urine. Smoky; acid; 1015; albumin, 0.4 per cent. Sediment: numerous hyaline and granular casts; epithelial casts; red blood-corpuscles; round epithelial cells; few leucocytes.

There was slight fever on November 4th and 5th, disappearing immediately under treatment with quinine 0.325 (gr. v) every four hours, which was discontinued on the 15th. The patient was placed on a milk-diet and given frequent hot-air baths. For five days the quantity of urine varied between 500 and 1200 c.c., after this date being above the normal quantity. The albumin rapidly diminished in amount, the œdema at the same time disappearing. On the 18th a faint trace of albumin was present and a few granular casts; a few red blood-corpuscles were still to be found. On the 23d the patient was discharged, apparently well.

CASE VI. Estivo-autumnal malarial fever; acute hemorrhagic nephritis; recovery (?).—No. 13,578. J. T., aged twenty-one years, was admitted August 13, 1895. Family history good; no previous illness beyond an attack of chills and fever two years ago, lasting three weeks. For three weeks has had daily chills and pain in the head and abdomen.

Physical examination. Marked pallor; no cardiac hypertrophy; no increase in pulse tension; spleen palpable.

Blood. Estivo-autumnal parasites; hyaline bodies and crescents.

Urine. Smoky; acid; 1012; trace of albumin. Sediment: dark-brown, flocculent, showing microscopically blood and pus cells, and hyaline and granular casts with blood adherent.

There were febrile paroxysms on the 13th and 14th, disappearing immediately under quinine, which was begun on the 14th—0.65 (gr. x), two doses, and then 0.325 every four hours. The urine increased in quantity; the albumin diminished, but was still present as a trace, with occasional hyaline, granular casts, and red blood-cells in the sediment on the day of discharge. On August 19th the patient, feeling perfectly well, left against advice. Beyond quinine, iron, in the form of Blaud's pills, was the only medicinal treatment.

CASE VII. *Malarial fever; aestivo-autumnal infection; cachexia; acute nephritis; recovery.*—No. 14,527. M. J. M., female, aged twenty-nine years. Admitted November 18, 1895. Family history negative. Scarlet fever, with dropsy, seventeen years ago; syphilis two years ago; otherwise always well and strong. Chills and fever, her first attack, off and on for seven months; frequent headaches; general debility. For three weeks moderate œdema of the face and legs.

Physical examination. Marked anæmia (1,160,000 red corpuscles) and cachexia. *Heart.* Apex just outside nipple in fifth space; soft blowing murmur all over cardiac area, lost in the axilla; no increase in pulse tension; spleen much enlarged.

Blood. Aestivo-autumnal parasites; hyaline bodies, crescentic and ovoid forms.

Urine. Cloudy; acid; 1006; decided trace of albumin; heavy brownish precipitate. Microscopically, numerous pus cells and granular casts with epithelial cells adherent.

There was irregular fever on the 18th and 19th, disappearing rapidly under quinine, 0.325 (gr. v) three times a day. The diet was restricted, and iron in the form of Blaud's pills was given.

The urine was increased in quantity throughout, and showed always a trace of albumin with a sediment as above, excepting for the occasional presence of a few red blood-corpuses.

The œdema disappeared, and on December 10th the patient left the hospital against advice, feeling greatly improved.

On January 27, 1896, patient returned complaining of severe nocturnal headaches which were of luetic origin, and disappeared in two weeks under iodide of potassium. The anæmia was much improved; red blood-corpuses 3,300,000.

Urine. Somewhat increased in quantity; still contains about 0.5 per cent. of albumin. The sediment showed hyaline and granular casts with occasional epithelial cells adherent.

The patient was again in the hospital in April, 1898, suffering from syphilitic periostitis. The urine throughout was normal; excretion of solids and urea normal; no albumin; no polyuria.

CASE VIII. *Malarial fever; obstinate quartan infection; acute nephritis; recovery (?).*—No. 16,720. R. M., aged twenty-two years, colored. Admitted July 19, 1896. Family history negative. Measles and whooping-cough as a child. Lived in a malarious district; has had chills and fever off and on for many years, more or less steadily for a year. For several months there has been frequent micturition, for four weeks œdema of feet and legs.

Physical examination. Marked pallor; no cardiac hypertrophy; no increased pulse tension; spleen palpable.

Blood. Triple quartan infection.

Urine. Pale yellow; neutral; 1010; albumin abundant; sediment; few leucocytes and red blood-corpuses; hyaline casts. .

The paroxysms, quartan in character, disappeared rapidly after quinine,

0.325 (gr. v), every four hours, which was begun on the 24th. The œdema rapidly diminished, and had entirely disappeared on discharge, excepting for a slight puffiness about the eyes. The *urine* throughout was increased. The albumin and casts rapidly diminished in quantity, but there was still a trace of the former on discharge.

The patient left against advice on July 30th, considering himself well. Besides quinine, the only medicinal treatment was with iron in the form of Bland's pills.

CASE IX. *Malarial fever; æstivo-autumnal infection; acute hemorrhagic nephritis; recovery.*—No. 16,832. W. E., colored, male, aged forty-two years. Admitted July 30, 1896. Family history negative. Measles, mumps, and whooping-cough as a child; pneumonia twenty-four years ago. For nine days, weakness, nausea, exhaustion. Syncopal attack two days ago; ischuria; frequent micturition.

Physical examination. Color good; tongue coated; no cardiac hypertrophy; apex impulse in the fifth space within the nipple line; no increase in pulse tension; spleen not palpable.

Blood. æstivo-autumnal parasites; hyaline, amoeboid, and ring-shaped forms.

Urine. Deep red; acid; 1030; marked trace of albumin; sediment, considerable; pus and red blood-corpuscles; hyaline and granular casts; small, round epithelial cells.

There were febrile paroxysms on the 30th and 31st, which disappeared immediately under quinine, 0.325 (gr. v), every four hours. The patient left the hospital apparently well on August 8th. There was no marked polyuria. Unfortunately, no further record was made of his urine.

The patient was seen again on April 16, 1898. Has been perfectly well since discharge. Is convalescent from a mild attack of acute bronchitis.

Heart's apex in sixth space 10 cm, from the median line, about in the mammillary line. Pulse tension not increased. Radial artery very slightly thickened.

Urine, passed at 11 A.M.; high color; acid; 1026½; no albumin by nitric acid or heat. Sediment; numerous cylindroids; small round cells; occasional red blood-corpuscles; a few hyaline casts with an occasional degenerated cell adherent.

CASE X. *Malarial fever; æstivo-autumnal infection; acute hemorrhagic nephritis; recovery.*—No. 16,995. A. H., male, aged thirty-five years. Admitted August 13, 1896. Family history negative. Measles, scarlet fever, and small-pox in childhood; renal colic nine years ago. Has complained for three days of severe headache, general exhaustion, and fever; has never had malarial fever previously.

Physical examination. Patient has high fever; is flushed; tongue coated; no cardiac hypertrophy; no increase in blood tension; spleen palpable.

Blood. æstivo-autumnal parasites; hyaline amoeboid bodies.

Urine. Dark; smoky; 1030; acid; trace of albumin; sediment slight. Microscopically, red blood-corpuscles, granular and hyaline casts.

There was high continued fever from the 13th to the 16th, after which date the temperature was normal following treatment with quinine, 0.325 (gr. v), every four hours, which was begun on the morning of the 14th.

The patient left on the 18th, feeling well. Unfortunately, no further note was made upon the urine.

The patient has been seen on a number of occasions since that time. Has had no further attacks of malaria, and believes that he is in perfectly good health. A specimen of urine obtained in June, 1898, was quite normal.

CASE XI. *Malarial fever; æstivo-autumnal infection: acute nephritis; recovery.*—No. 17,000. J. P., female, colored, aged forty-four years. Admitted August 13, 1896. Family history negative. Measles, mumps, and whooping-cough as a child. Has had several previous attacks of chills and fever. For about two weeks has complained of vomiting, headache, and at times slight delirium; ischuria.

Physical examination. Large woman; tongue coated; no anasarca; fine râles at bases of the lungs; slight accentuation of second aortic sound; no apparent cardiac hypertrophy; no increased pulse tension; spleen not palpable.

Blood. Æstivo-autumnal parasites; amoeboid hyaline bodies and crescents.

Urine. Amber; acid; 1025; albumin 0.2 per cent. Sediment: pus and vaginal epithelium, hyaline and granular casts.

There were febrile paroxysms on the 13th, 14th, and 15th, disappearing rapidly under quinine. The patient left the hospital on August 22d, at her own request, feeling perfectly well. Unfortunately, no final note was made upon the urine.

The patient was communicated with by letter, and states on April 10, 1898, that she is perfectly well. She has, however, had chills and fever since leaving the hospital. A specimen of urine obtained in May, 1898, was absolutely normal in character.

CASE XII. *Malarial fever; æstivo-autumnal infection; nephritis; recovery.*—No. 17,071. C. S., aged twenty-seven years; male. Admitted August 21, 1896. Family history negative. Has had no serious illness. The patient never suffered from malarial fever previously; he lives in a malarious district. Seven weeks ago began to suffer with swelling of the abdomen and legs, for which he took to bed. Since then the swelling has become general.

Physical examination. Yellowish complexion; marked pallor; no cardiac hypertrophy; slight accentuation of the second aortic sound; spleen palpable; marked œdema of the legs.

Blood. Æstivo-autumnal parasites; numerous crescentic and ovoid forms.

Urine. Light amber; 1012; trace of albumin; numerous hyaline and granular casts with epithelium adherent; epithelial casts; yellow granular casts, suggestive of a blood staining.

There was moderate fever on admission, rapidly disappearing under quinine, 0.325 (gr. v), every four hours, which was begun on August 23d. The patient was placed on a milk diet and given bitartrate of potassium as a diuretic.

The quantity of urine up to September 11th was above normal, averaging over 2000 c.c., the albumin diminishing in quantity. Occasional blood-corpuscles were also seen in the sediment and upon the casts.

On the 16th, without apparent cause, the urine fell to 600 c.c. There were pain and swelling of the left knee-joint.

17th. Urine reddish; smoky; albumin 0.15 per cent. Sediment, numerous blood-corpuscles and an increased number of casts.

From this date the urine steadily improved, the quantity being throughout supranormal. The patient improved progressively; the swelling and pain in the knee rapidly disappeared.

Oct. 21st. Urine: 3000 c.c.; pale; acid; 1010; no albumin; sediment shows nothing abnormal. Patient discharged well.

CASE XIII. *Malarial fever; æstivo-autumnal infection; acute hemorrhagic nephritis; recovery.*—No. 17,250. M. S., female, aged ten years. Admitted September 9, 1896. Family history negative. Has had measles. Lives in a malarial district, and has had chills before. One week ago she began to have fever, abdominal pain, and headache. There were two chills at the onset; these were followed by swelling of the abdomen and legs.

Physical examination. Marked pallor; general œdema and ascites. No cardiac hypertrophy; blood tension not increased; spleen palpable.

Blood. Æstivo-autumnal parasites; crescentic forms.

Urine. Smoky; acid; 1015; 0.2 per cent. albumin. Sediment, pus, hyaline, granular and blood casts; red blood-corpuscles.

There were febrile paroxysms on the 10th, 11th, and 12th, disappearing immediately after quinine, 0.26 (gr. iv), three times a day, on the 13th. The patient was given a milk diet, and bitartrate of potassium as a diuretic.

The œdema slowly disappeared. It was last noted on the 29th of September. The urine, at first reduced in quantity, soon became increased above the normal amount; the albumin diminished to a slight trace.

Oct. 24th. Urine pale; acid; 1012; albumin 0.1 per cent. Sediment, few granular and hyaline casts; several red blood-corpuscles.

Oct. 25th. The patient was discharged to-day feeling perfectly well.

See subsequent history, Case XVIII.

CASE XIV. *Malarial fever; æstivo-autumnal infection; acute hemorrhagic nephritis; carbuncle; left the hospital improved.*—No. 17,266. H. J. S., aged forty-one years. Admitted September 11, 1896. Family history good. Measles as a child; syphilis eight years ago; malaria seven years ago.

The patient has had daily chills off and on for a month, the last twelve days ago; this is his first attack. Ten days ago, after exposure, œdema of the face and extremities appeared. Afterward he began to suffer with pain in the neck.

Physical examination. Marked pallor; general œdema; ascites; no cardiac hypertrophy; carbuncle on the back of the neck; heart sounds normal; arteries slightly thickened; spleen not palpable.

Blood. Æstivo-autumnal parasites; hyaline bodies; presegmenting forms; crescentic bodies.

Urine. Dark red; acid; 1017; albumin abundant. Sediment, heavy, brownish; granular, epithelial, blood, and pus casts; epithelial cells; leucocytes; red blood-corpuscles.

There were slight evening elevations of the temperature on the 11th, 12th, and 13th. On the 14th the patient left the hospital against advice; operation upon the carbuncle having been advised. The patient was much improved, the oedema having almost disappeared.

CASE XV.—*Vide page 18.*

CASE XVI.—*Vide page 18.*

CASE XVII.—*Vide page 24.*

CASE XVIII. *Malarial fever; double tertian infection; acute hemorrhagic nephritis; recovery.*—No. 19,288. M. S., female, aged eleven years. Admitted April 27, 1897. The patient, who had suffered from a similar attack in September, 1896 (Case XIII.), had been enjoying good health since her discharge from the hospital.

Seventeen days ago she began to have tertian chills, which have continued since. There have been frequent attacks of nausea and vomiting and vertigo.

Physical examination. Marked pallor; face puffy; heart and lungs negative; spleen palpable.

Blood. Two groups of tertian parasites.

Urine. Smoky; acid; 1015; trace of albumin. Sediment, moderate; small epithelial cells, hyaline and granular casts, one with a considerable quantity of fat; few leucocytes; occasional red blood-corpuscles. Febrile paroxysms occurred on the 27th and 28th, disappearing after treatment by quinine, 0.13 (gr. ii), every four hours.

The patient improved rapidly, the smokiness disappearing soon from the urine. The oedema of the eyes rapidly subsided.

May 4th. Urine. Pale; acid; 1012; faint trace of albumin. Sediment, slight; epithelial cells; few small hyaline casts.

5th. Patient, feeling perfectly well, leaves the hospital against advice.

On May 17th the patient returned to the hospital, having had a chill two days before, after which she had taken quinine. The blood was free from parasites and no further chills occurred; the treatment was continued.

Physical examination was negative.

The *urine* was examined frequently during the next two weeks; it was always perfectly normal. The urea, estimated on one occasion, amounted to 0.028 per c.cm. On June 2, 1897, the patient was discharged, well.

CASE XIX. *Malarial fever; aestivo-autumnal infection; acute hemorrhagic nephritis; recovery (?).*—No. 20,421. J. P., male, aged thirty-eight years, was admitted August 25, 1897. Family history good; no history of infectious diseases. The patient had chills as a child and again last year. For four weeks he has suffered from chills and fever off and on; for three weeks there have been swelling of the legs and abdomen, drowsiness, ischuria, dyspnoea.

Physical examination. Pallor; general oedema and ascites; double hydrothorax; no cardiac hypertrophy; pulse tension rather high; spleen not palpable.

Blood. Æstivo-autumnal parasites; hyaline amoeboid bodies; crescentic forms.

Urine. Deep amber; slightly turbid; acid; 1020; albumin abundant. Sediment, flocculent; hyaline casts, with epithelium, pus, and blood adherent; free blood and pus.

There were febrile paroxysms on the 25th and 26th, the temperature remaining normal after the beginning of quinine—0.325 (gr. v) three times a day—on the 27th. The œdema and ascites rapidly disappeared.

The urine was reduced in quantity on the 26th and 27th (880 and 560 c.c.). From this time on there was polyuria, amounting to 2200 c.c. on September 1st. The albumin steadily diminished in quantity. On September 2d the urine was of normal color; acid; 1015; no albumin; microscopically, a few hyaline casts are still to be found in the sediment. The patient left the hospital, against advice, feeling perfectly well.

CASE XX.—*Vide page 25.*

CASE XXI.—*Vide page 26.*

CASE XXII. *Malarial fever; type ?; acute nephritis; recovery(?)*.—L. S., male, colored, aged forty-three years, visited the out-patient department on March 27, 1895. Family history negative; measles and whooping-cough as a child; chills and fever in spring of 1894. For three weeks he has complained of cough and expectoration; for three days he has had chills and swelling of the legs; frequent micturition.

Physical examination. Pallor; œdema of the legs; harsh breathing, with fine crackling râles at the apex of the right lung.

Blood. Malarial parasites found; type not mentioned.

“*Urine.* Albuminous ring quite marked with HNO_3 .”

Treatment. Quinine.

April 10, 1895, feels better in every way.

CASE XXIII. *Malarial fever; tertian infection; acute nephritis; result (?)*.—K. W., female, aged seventeen years, visited the out-patient department on July 31, 1896. Family history negative; has had measles, otherwise no serious illness. The patient has had chills previously. For ten days there have been daily paroxysms.

Physical examination. Tongue coated; nasal and labial herpes; spleen palpable.

Blood. Partially grown tertian parasites.

August 14th. Chills have disappeared, but a week ago noticed œdema of the feet; scantiness of urine.

The urine contained large amount of albumin; hyaline and granular casts; numerous bladder and vaginal epithelial cells.

Treatment. Milk diet, rest in bed, quinine.

The patient did not report again.

CASE XXIV. *Malarial fever; tertian infection; acute nephritis; recovery(?)*.—F. G., female, aged twenty-three years, visited the dispensary August 17, 1896. Family history negative; has had no serious illness. The patient has never had malarial fever; for a day or so, very severe headache.

Physical examination. Marked pallor; moderate œdema of the legs.

Urine. Decided trace of albumin; epithelial cells; leucocytes; numerous coarsely and finely granular casts.

August 22d. Returned to-day, complaining of having had three tertian chills, the last on Sunday; severe headache.

Blood. Tertian parasites; half-grown forms.

Under quinine the patient made a perfect recovery. Seen again March 17, 1897, feeling perfectly well. No further examinations of the urine were recorded.

CASE XXV. *Malarial fever; æstivo-autumnal infection; acute hemorrhagic nephritis; result (?).*—J. S., aged twenty-one years, visited the out-patient department September 28, 1897. Family history negative; measles as a child. The patient had never suffered from malaria previously. Two weeks ago two chills; since then swelling of the face and legs came on, and he has complained of bad taste in the mouth.

Physical examination. General œdema; no cardiac hypertrophy; spleen palpable.

Blood. Æstivo-autumnal organisms; numerous crescents.

Urine. Smoky, bloody; contains a large quantity of albumin.

Treatment. Advised to enter hospital. The patient did not return.

CASE XXVI. *Malarial fever; æstivo-autumnal infection; acute nephritis; arterio-sclerosis.*—J. M., aged forty years, visited the out-patient department October 20, 1896. Family history negative; always strong and well. For four weeks and a half the patient has had chills off and on, his first attack; headache, vertigo, and swelling of the feet for a week.

Physical examination. Pallor; œdema of the legs; apex impulse under the sixth rib in mammillary line; sounds clear; radial arteries thickened.

Blood. Æstivo-autumnal parasites; numerous crescentic bodies.

“*Urine* has marked amount of albumin.”

The patient refused to enter the hospital and failed to report at the dispensary again.

